

CINCHONA BARK AND ITS ALKALOIDS.

THE Chadwick Trustees had the happy idea of asking Sir David Prain to give a lecture on the economic and hygienic relationship of cinchona bark and its alkaloids, in the Chelsea Physic Garden. The review we published a few weeks ago¹ of Dr. Dawtrey Drewitt's *The Romance of the Apothecaries' Garden at Chelsea* was full enough to prove the place appropriate; and that the lecturer was well chosen is proved by the fact that before he became director of the Royal Botanic Garden, Kew, a post he held for some eighteen years, and while on the active list of the Indian Medical Service, Sir David Prain was director of the Botanical Survey of India and Superintendent of the Royal Botanic Garden, Calcutta.

The lecture, which was given on the afternoon of June 4th, afforded to many an opportunity of visiting a secluded corner of London with which few even of those who profess to know the great city well are acquainted.

SIR DAVID PRAIN said that European acquaintance with Peruvian bark was to be traced to an illness in 1638 of a Vicereine of Peru, the Countess of Chinchon, after whom the genus *Cinchona* is named. This bark was thereafter exploited as a forest product in the province of Loxa, now Southern Ecuador. It found a place in a London pharmacopoeia for the first time in 1677.

The exploitation of forest products led to an increase in price, to contraction of supplies, and to a search for substitutes. After 1753 the red bark of *C. succirubra* from Chimborazo in Northern Ecuador competed with the pale bark of *C. officinalis* from Loxa, which now was placed on the market as genuine or crown bark. But red bark by degrees replaced crown; it became, and still is, the only cinchona bark treated as official. In the bark trade substitution was repeated at intervals; the grey bark of *C. micrantha* and *C. nitida*, from Huanuco in Central Peru, competed with red. Later the yellow bark of *C. Calisaya* from Bolivia competed with grey, and after yellow became scarce the Colombian bark of *C. lancifolia* was exported. Colombian was the last of the South American cinchona barks of importance to pharmacy; Europe had therefore to undertake the cultivation of cinchona.

Various limiting factors (Sir David Prain continued) govern the conversion of forest products into crops. If labour is not available locally a crop must go where labour is. France tried cinchona in Algeria in 1849; Holland did so in Java in 1851; England followed in Ceylon, the Nilgiris, and the Eastern Himalaya in 1861.

Another factor is environment. The climate and soil of Algeria were inimical to cinchona; those of Java were satisfactory. Ceylon and South India supplied a suitable climate but an indifferent soil; the Eastern Himalaya has a climate marred by the occurrence of a distinct dry season.

A third factor is adaptability. Colombian bark does not thrive well, even in Java. Red and grey both prove accommodating, even in the Himalaya. Yellow can be raised in the Eastern Himalaya but not in South India.

There are limiting factors connected with use as well as with production. In the Andes rain-forests there are forty cinchonas; only some six of these have yielded bark of importance to pharmacy. In these important barks the alkaloid content may vary; 3 per cent. means a poor, 6 per cent. a good, 9 per cent. or over a rich sample. This natural variation may be increased by environment; a strain with bark "good" in Java may have bark "poor" in South India or the Himalaya. The factor of alkaloid content, though a limiting one, need not inhibit cultivation; it does, however, involve careful selection of strains. But the factor of allied alkaloid nature is more important; under existing conditions it involves the selection of particular kinds of cinchona bark.

The alkaloids of cinchona may be amorphous or crystallizable. All are remedial against malaria. The physiological action of the amorphous is, however, the more rapid, and the efficacy of the crystallizable alkaloids is increased when they are administered in an uncrystallized state.

The crystallizable alkaloids in official cinchona bark

were first separated in 1815. This derivative, "cinchonino," was found in 1820 to yield a definite alkaloid, quinine, and something more. By 1852 this "something" was shown to include the crystallizable alkaloids cinchonidine, cinchonine, and quinidine.

As compared with the variable percentage of alkaloids in a particular kind of cinchona bark, the proportion of these alkaloids to each other remains relatively stable. In any sample of official red bark we may expect one-half the alkaloid content to be cinchonine, one-third quinine, one-sixteenth cinchonidine, only one-eightieth quinidine; the remainder—about one-eighth—is amorphous. But the proportions differ in different kinds of cinchona bark. Though quinine constitutes but one-third of the total alkaloid content in red bark, it forms three-fourths in crown bark. Yellow bark may be richer in quinine than crown; grey is poorer in quinine than red. By 1820, when quinine was first isolated, yellow bark was that most used in pharmacy; quinine became, and still remains, the only alkaloid of cinchona bark that is official.

As the only official alkaloid, quinine is that commonly prescribed for use against malaria. It is therefore also the one chiefly separated from cinchona bark. So marked is the effect of this fact that the purchaser of cinchona bark pays for it in terms of its quinine content. But its costs about as much to work up a bark with a poor quinine content as it does to treat one with a high quinine content, and the latter finds a market before the former. It also costs about as much to cultivate and harvest a cinchona with little quinine as one with much, and the planter who can raise yellow bark, which may have five-sixths of its alkaloid content quinine, will grow this in preference to crown, where only three-fourths of the alkaloid content is quinine. These economic relationships of cinchona bark and its alkaloids are often misunderstood. It has been said that the abandonment of cinchona cultivation in Ceylon took place because "cinchona planted without scientific advice began to deteriorate"; that the industry was abandoned by private enterprise in South India owing to the establishment of a cinchona monopoly by the Dutch in Java. In Ceylon the cultivation of coffee had to be given up owing to disease. Coffee was replaced by cinchona. But Ceylon cannot, like Java, grow yellow bark; she can only, like South India, grow crown. As soon as Ceylon found that her return for the same outlay was inferior to the return obtained by Java, Ceylon abandoned cinchona and took up tea. The corresponding abandonment of cinchona by private enterprise in South India has been due to the fact that yellow bark, which cannot be grown there, thrives better in Java than in any region outside Bolivia in which it has been tried. The so-called cinchona monopoly of Java, if a monopoly at all, was a quinine monopoly which was not the creation of Holland. The necessity to grow yellow bark in preference to other kinds is an economic consequence of the accident that medicine regards the hygienic relationships of quinine as being unlike those of the other alkaloids of cinchona bark.

It is not impossible that the conditions whose effects have been mistaken for a Dutch monopoly are responsible for complaints now current as to a world shortage of quinine. Manufacturers of that drug, who might be supposed to know the facts, seem disposed to believe these complaints exaggerated. While would-be consumers and potential suppliers of quinine are discussing the situation as regards the alkaloid, the cinchona planter explains that he is less than satisfied with the price he receives for the bark he sells, and that it is not possible for him to market all the bark he can harvest. This suggests overproduction, not shortage; it shows that the Java planter, far from having obtained control of the output of quinine, has lost control of the output of cinchona bark.

We are more concerned, however, with the facts that the only cinchona it is possible to cultivate without financial loss is yellow bark, and that this has put it beyond the power of our Empire to supply its own requirements as regards quinine. Some do not think this a regrettable situation, on the ground that shortage of this remedy for malaria gives an impetus to the crusade against its cause. We can appreciate the feeling: prevention is better than cure. Others, however, hold the view that until prevention has

¹ BRITISH MEDICAL JOURNAL, May 3rd, 1924, p. 787.

been fully ensured, the provision of what is a reliable remedial agent remains a public duty. Medicine, therefore, urges the State to grow cinchona, wherever it can be grown, more extensively than is done at present.

This appeal by medicine might carry greater weight if fuller account were taken of the effect on the economic relationships of cinchona of those hygienic relationships of its alkaloids for which she herself is responsible. Medicine has not overlooked this altogether; she considers all the alkaloids of cinchona as worthy of use, so long as they remain unseparated from one kind of cinchona bark. It is only after the alkaloids have been extracted from their bark that medicine feels constrained to treat all but one of them as of no importance. Even if it were true that quinine, as a remedy for malaria, is more useful than its companion alkaloids, it remains for consideration whether the treatment of these other alkaloids as waste products of no value be wholly justifiable. It is to this action on the part of medicine that the economic relationships which now exist owe their origin. If medicine can see her way to some modification of her present attitude, conditions that hamper the State and distress its servants might disappear; full advantage could then be taken of cinchona bark and its alkaloids.

SOCIOLOGICAL ASPECTS OF MENTAL DISORDER.

THE MAUDSLEY LECTURE.

THE fifth Maudsley Lecture, before the Medico-Psychological Association of Great Britain and Ireland, was given by Dr. JOHN CARSWELL in the Barnes Hall of the Royal Society of Medicine, on May 22nd, with the President, Dr. EDWIN GOODALL, C.B.E., in the chair. The subject of the lecture was "Some sociological considerations bearing upon the occurrence, prevention, and treatment of mental disorders."

Dr. Carswell said that the freedom from restraint and provision for open-air life of patients in Scottish asylums was due in no small measure to the courage and initiative of James Rutherford. Courage was needed in this domain, for the public suspected that any departure from convention in this branch of medicine was a menace to security. Arthur Mitchell secured the establishment of the boarding-out system for chronic harmless patients, and the General Board of Control had generated an open-mindedness towards new methods which had reassured the public. The lecturer had proposed for Glasgow machinery for placing the certification of alleged insane persons in charge of one medical officer, and securing provision for the treatment of suitable cases, without certification, in observation wards. The proposals received the approval of the General Board of Lunacy and of the Local Government Board. That scheme was put into operation, and was now in full working order. There was no power of compulsory detention. Glasgow parish, with a population of 600,000, was also the lunacy district, and the parish council, as such, administered the Poor Law, and as District Board of Control it provided and controlled asylum accommodation and treatment. There was, therefore, no conflict of interest or official overlapping. The intention was to ensure that no one should be placed under lunacy certificate who could be treated successfully otherwise. It became possible, under the scheme, to make a systematic investigation into the occurrence of insanity, especially in relation to local, economic, and social conditions. It was the results of this investigation the lecturer proposed to present in the course of his address. He projected on to the screen a table showing, in this community of 600,000, first attacks of insanity during each year from 1901 to 1913, and the proportion per 10,000 of the total population. The numbers ranged from 364 to 443, and the number per 10,000 from 5.6 to 7.7. The figures showed a steady rate; they included a number of idiot and imbecile children. He then divided the cases into two age-periods—15 to 45, and over 45 years—and gave the proportion per 10,000 of the population. Those in the first period embraced half the total population. There was little difference in the proportions in the two sexes. This active period, 15 to 45 years, gave a general average first attack rate of about

8 per 10,000 of population. At the ages of over 45 years the male rate ranged from 12.6 to 20, and the female rate from 13.2 to 16.1.

Dr. Carswell's next inquiry was as to how the figures were related to the physical conditions of the people concerned. There were 909 cases of which the cause of the mental condition was ascertained, and he placed them in five groups. He exhibited the table, as follows:

	Age 15-45.	Age over 45.	Total.
GROUP I. Constitutional instability ...	358	35	393
GROUP II. Toxic	152	96	248
GROUP III. Gross organic brain disease...	10	51	61
GROUP IV. Senile changes	—	189	189
GROUP V. All other causes	15	3	18
Totals	535	374	909
Percentage of total ascertained causes	58.8	41.2	

The figures showed that 67 per cent. of the cases occurring at ages between 15 and 45 were based upon some constitutional morbid process, and this was the most constant element in the annual production of insanity at those ages. Of all the cases at all ages 43 per cent. had a constitutional basis, and 27 per cent. at all ages were caused by syphilis, alcohol, or exhaustion states. In 50 per cent. of cases at ages over 45 senility was found to be the most prominent causative element.

Pursuing the inquiry, he next showed the incidence of first attacks of insanity in two area groups: that with a death rate above the rate for the whole city; and secondly, that with a death rate below the city average. The period taken for this was 1911-13.

Area Group.	Population.	Ages 15-45.	Ages over 45.	Total.
I. Above average	199,000	186	149	335
II. Below average	198,000	165	91	256

The large number of cases which occurred at over 45 years of age in Group I pointed to economic and other social factors which acted more powerfully in poor and unhealthy districts than in places more favourably circumstanced. The practical similarity of the occurrence of insanity at ages 15-45 in both areas was noteworthy.

The important question arose as to how far the possession of observation wards kept down the number of persons certified as lunatics. He replied that many people who required treatment but would not have reached a mental hospital as certified patients because of sentimental objections accepted this provision for their care, and a considerable number of persons were expedited on their way to asylum care by having this probationary care, which care satisfied their relatives that further treatment was needed. He had no doubt that large numbers of patients were treated to a state of recovery who otherwise would have had to be certified. He projected the following informing tabulation:

	Males.	Females.	Total.
Total cases admitted... ..	3,487	2,923	6,410
Discharged Cases:			
Recovered	1,496	1,097	2,593
Improved	593	520	1,113
Certified Insane	1,163	1,128	2,291
Died	216	163	379
Total cases discharged and died	3,468	2,908	6,376
Remaining on May 15th, 1914 ...	19	15	34